

CEPI

The  
urgency  
of now

Turning the tide against epidemic and pandemic infectious diseases



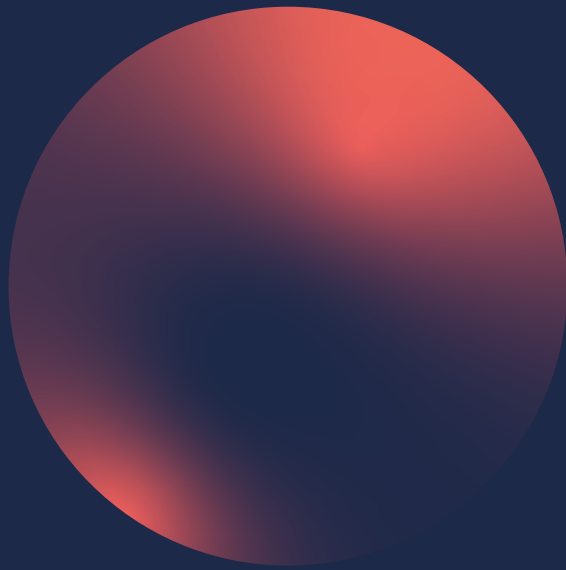
COVID-19 has killed millions and destroyed the livelihoods of hundreds of millions of people. By the end of 2025, it will have cost the global economy \$28 trillion.



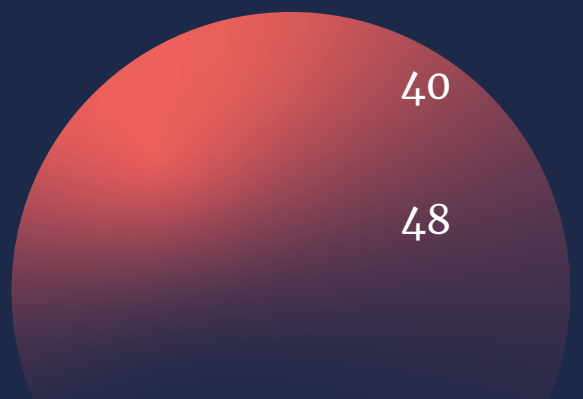
**We can  
never let  
this happen  
again**


We have the tools. We know what we need to do. For the first time in history, we can credibly aim to eliminate the risk of epidemics and pandemics. We must invest in the vaccines and biologic countermeasures that we will need, while ensuring that no one is left behind. Our goal is within reach. We need only seize the fierce urgency of now.

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**A \$3.5 billion  
plan of action**

In 2020 the world was brought to its knees by an invisible enemy, COVID-19. Entire economies went into lockdown. Trillions of dollars were wiped from global markets, hundreds of millions of jobs lost, decades of development gains swept away. By early 2021, more than a hundred million people had been infected and more than two million had died. The ripple effects of this devastating pandemic will be felt for generations. It is vital that we capitalise on the rare alignment of political will, practical experience, and technical and scientific progress emerging from the pandemic to prevent such devastation happening again.

But if we do nothing, it will—and perhaps soon. We were fortunate, in a way, that COVID-19 was caused by a coronavirus and that we could build on years of work on vaccines against related coronaviruses to rapidly develop highly effective vaccines against it. However, developing vaccines against a new pathogen—one that mutates quickly, is highly transmissible, and deadly—could take much longer. Even COVID-19 is becoming problematic for our latest vaccines, because of the emergence of new variants, which can reinfect people who have been infected before and are already rendering our countermeasures—including our vaccines and monoclonal-antibody treatments—substantially less effective or useless.

As COVID-19 has so amply demonstrated, emerging infectious diseases represent an existential threat to our way of life. It was not the first and, unless we take dramatic action, will not be the last pandemic of the 21<sup>st</sup> century. But unlike some of the other big threats that humanity faces, we have the tools to substantially reduce and even to eliminate the risk of future pandemics. A decade ago such an ambition would have seemed utopian; now, having compressed a decade of technology development into less than 12 months, it is well within our grasp—if we take action.

CEPI is seeking to raise \$3.5 billion to implement CEPI's next 5-year plan. To mitigate the immediate threat of COVID-19 variants, it is activating key elements of this plan now—and seeking to mobilise a portion of this \$3.5 billion in 2021. We have already launched R&D programmes to initiate development of next-generation vaccines against COVID-19 variants and we are planning studies to answer critical scientific questions related to the durability of immunity, effectiveness of mixed-vaccine regimens, and vaccine effectiveness in vulnerable populations such as pregnant women. We are also bringing forward our plans to develop vaccines that could protect against multiple COVID-19 variants and other coronavirus species.

For countries seeking to expand their investments in health security, CEPI can offer a global focus, a proven track record, the agility to move

quickly, and extensive multisectoral partnerships. CEPI is also able to leverage its unique connecting role—as a coalition of vaccine developers, manufacturers, sovereign governments, philanthropies, civil society and global health organisations—and extensive networks to pool and deploy resources in ways that nation states often cannot.

The important role that CEPI is playing in responding to COVID-19 shows that it is well positioned to assemble the capabilities, actors, and expertise needed to develop vaccines, promote equitable access, and create new and effective multisectoral partnerships.

Building on the strong achievements and foundations laid down in its first 5 years, CEPI will initiate a series of ambitious programmes, described below, to substantially reduce global epidemic and pandemic risk.



**Epidemic and pandemic diseases should be viewed not merely as a public health risk but as an existential threat to modern society. They are a transnational threat that demands a coordinated and collective global response.**

*Dr Richard Hatchett, CEO of CEPI*



### **Compressing vaccine development timelines to 100 days**

During COVID-19, the time from the release of the SARS-CoV-2 genetic sequence to the first emergency authorisation by a stringent regulatory authority of a COVID-19 vaccine was 326 days. But against a threat such as COVID-19, this was far too long. Our aspiration will be to develop a safe and effective vaccine in 100 days (figure 1).

Had this timeline been achieved during the COVID-19 pandemic, regulatory review would have begun in April 2020, 7 months faster than the 10½ months achieved by Pfizer/BioNtech with their mRNA vaccine. A vaccine could have been ready for emergency use much sooner, potentially averting millions of deaths and trillions of dollars in economic damage. Instead of the first injections occurring on December 8, 2020, when more than 67 million cases had been confirmed, they might have begun on May 8, when fewer than 3.8 million cases had been recorded.<sup>1</sup>



Shortening emergency vaccine development timelines to this extent will require substantial prior investment in the development and testing of vaccine candidates against prototype pathogens; deep familiarity and comfort of regulators with the leading platform technologies; rapid publication of genetic sequences; tight coordination of specimen collection and dissemination; clinical trial protocols and networks at the ready; precise execution of each step of the development process; and the use of pre-identified manufacturing capacity.

100-day vaccine development is ambitious, but it is what we must achieve if we are to break the cycle of epidemics and pandemics stalking humanity.



## Reducing the threat posed by coronaviruses

Coronaviruses have now demonstrated their pandemic potential. The coronaviruses that cause Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) are associated with case fatality rates of 10–35% (5–16 times worse than COVID-19) and we know that coronaviruses circulate widely in animal reservoirs. The emergence of a coronavirus combining the transmissibility of COVID-19 with the lethality of SARS or MERS would be civilization-shattering. Eliminating the threat posed by coronaviruses is thus an issue of the greatest global urgency.

CEPI will, therefore, initiate a programme to develop vaccines that provide broad protection against coronaviruses with the ultimate objective of developing vaccines that provide broad protection against SARS-CoV-2 variants and vaccines that provide broad protection against *Betacoronaviruses*. CEPI will build on the vaccine technologies validated in the COVID-19 response to advance our understanding of coronavirus immunology and viral evolution and enlist structural biologists to identify the viral family's weak points. CEPI anticipates that developing broadly protective *Betacoronavirus* vaccines will be a shared global priority and will work closely with partners to advance work in this area as quickly as possible.

CEPI initiated its efforts to prepare for future coronavirus threats by launching a collaboration with the GISAID Initiative, Public Health England, and the National Institute for Biological Standards and Control to strengthen real-time global tracking and testing of COVID-19 sequences. In the context of this virus, this system will be crucial in monitoring the emergence of mutant strains of the virus (such as B.1.1.7, B.1.351, and P.1 strains). Strains with mutations or changes in biologically significant regions of the virus will be tested to determine whether they are likely to have any impact on vaccine effectiveness or naturally derived immunity. Monitoring the evolution of the virus over time will inform the development of next-generation vaccines and strategies for managing the virus as it becomes endemic.

## Developing a library of vaccine candidates to speed up vaccine development

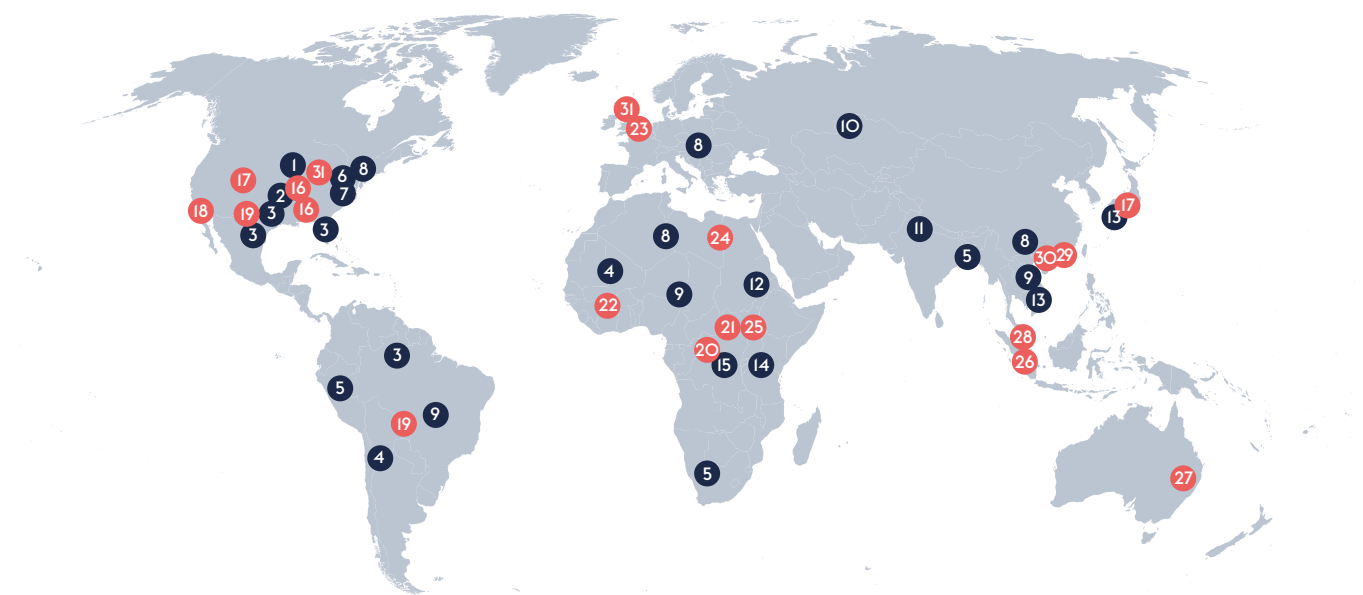
Around 260 viruses from roughly 25 viral families are known to infect humans, and the Global Virome Project estimates over 1.6 million yet-to-be-discovered viral species to exist in mammal and bird hosts—the most important reservoirs for viral zoonoses (figure 1).<sup>2</sup>

We cannot develop vaccines against all potential viral threats, but we can produce a library of prototype vaccines and other biological countermeasures against representative pathogens from these critical viral families.

Much as research into MERS, and development of vaccines against it, enabled the rapid advancement of vaccines against COVID-19, developing prototype vaccines against representative pathogens could greatly accelerate the development of vaccines against any newly emerging but related threats. By adopting this approach, we believe we can radically reduce R&D timelines for new vaccines while familiarising regulators with vaccines against related threats. We view the work on prototype pathogens as a critical enabler of our 100-day vaccine development aspiration.

Developing a library of vaccine candidates will require substantial financial investment and commitment of human resources. The selection of candidates will be critical and can be gradually expanded over time. To advance rapidly, this will need to be a shared and coordinated global project.

**FIGURE I:**  
The challenge of emerging and re-emerging infectious diseases



- |                                     |                                   |                                   |                       |
|-------------------------------------|-----------------------------------|-----------------------------------|-----------------------|
| 1. Vancomycin-resistant S.aureus    | 9. Drug-resistant malaria         | 16. Cyclosporiasis                | 24. Hepatitis C       |
| 2. Human monkeypox                  | 10. Diphtheria                    | 17. E. coli O157:H7               | 25. HIV               |
| 3. Dengue                           | 11. Typhoid fever                 | 18. Whitewater arroyo virus       | 26. Enterovirus 71    |
| 4. Yellow fever                     | 12. Rift Valley fever             | 19. Hantavirus pulmonary syndrome | 27. Hendra virus      |
| 5. Cholera                          | 13. Vancomycin-resistant S.aureus | 20. Marburg haemorrhagic fever    | 28. Nipah virus       |
| 6. Lyme disease                     | 14. Human monkeypox               | 21. Ebola haemorrhagic fever      | 29. H5NI influenza    |
| 7. West nile virus                  | 15. Plague                        | 22. Lassa fever                   | 30. SARS              |
| 8. Multidrug-resistant tuberculosis |                                   | 23. vCJD                          | 31. Cryptosporidiosis |

Red represents newly emerging diseases; blue, re-emerging/resurging diseases.<sup>3</sup>





Norway is proud to be a founding member of CEPI. With the pandemic, CEPI is more important than ever. Ensuring access to vaccines for all is a necessity, not a luxury. As the emergence of new variants tells us: no one is safe before everyone is safe. The mutations underline the need for a continued investment in vaccine development. Norway will continue to mobilise around CEPI and other much-needed building blocks in global health. If anything, the pandemic has reminded all of us that we need better preparedness and response. We have focused on this agenda for a long time. This is not the time to give up. You can count on Norway's continued support.

*Erna Solberg, Prime Minister of Norway*



CEPI's rapid response to COVID-19 suggests what can be achieved by this approach. When COVID-19 struck, CEPI was primed and ready to support vaccine development. The genetic sequence for SARS-CoV-2 was published on January 11, 2020. By January 23, CEPI initiated its first three programmes to accelerate development of vaccines against this novel pathogen, when just 581 cases of the virus had been confirmed worldwide.<sup>4</sup>

CEPI was able to move with such agility because it had already identified coronaviruses as serious threats and invested over \$140 million in the development of vaccines against MERS. Within a few weeks of the COVID-19 outbreak, most of CEPI's MERS vaccine development partners had pivoted to work on the new virus. CEPI had also previously invested over \$50 million in a rapid response programme—including mRNA vaccines—against novel pathogens. These programmes also pivoted to work on the new pathogen. From these initial investments, CEPI established the world's largest portfolio of COVID-19 vaccine candidates and worked with WHO and Gavi to make candidates within the portfolio globally accessible through COVAX to hasten the end of the acute phase of the pandemic by the end of 2021.

### **Protecting and empowering lower income countries**

While COVAX has been able to put agreements in place to enable access to more than 2 billion doses of COVID-19 vaccines for 191 participating and eligible economies in 2021, the devastation of the pandemic will still hit low-income and middle-income countries (LMICs) especially hard.

**CEPI has helped the global science community do something incredible: develop COVID-19 vaccines in less than a year. With the right support, CEPI will continue to accelerate innovation and achieve breakthroughs, helping ensure that everyone has equitable access to lifesaving vaccines.**

*Bill Gates, Co-Chair, Bill & Melinda Gates Foundation*



The fragile health systems in many of these countries and their limited means to finance or to drive vaccine development on their own puts LMIC populations at heightened risk. Therefore, there is an urgent need to work with these countries to build resilience and capacity to deal with such emerging infectious threats.

CEPI's vision is to assist LMICs with developing the infrastructure and expertise to undertake the epidemiological, enabling science, and clinical studies needed to advance vaccine development, support technology transfer, and strengthen national and regional manufacturing capacity, and engage with local and regional regulatory authorities that will enable such countries to take full ownership of their national health security.

By working with LMICs to connect national and regional R&D capacity and enabling equitable access to CEPI-supported innovations, we can also make a significant contribution to the Sustainable Development Goals (SDGs), specifically SDG 3—*Good Health and Wellbeing*. CEPI will also continue to support the development of vaccines against known high-risk pathogens such as Chikungunya, Ebola, Lassa Fever, MERS, Nipah, and Rift Valley Fever to assess their effectiveness and protect vulnerable populations.

As we've seen with COVID-19, emerging infectious diseases can threaten the health security and economic stability of both lower income and higher income countries alike. Therefore, CEPI's work to prevent and mitigate the effects of pathogens with epidemic and pandemic potential will complement the objectives of most other SDGs.

### **Why the world needs CEPI**

Now is the moment for the world to unite and break the cycle of panic and neglect that has characterised the historical response to epidemic and pandemic disease. COVID-19 has devastated the world, but it has also heralded a renaissance in global cooperation to accelerate the development of vaccines and other biologics against a shared threat.

As the world recovers from COVID-19, a *post-pandemic consensus* will emerge in which governments and the private sector make long-lasting commitments to global epidemic and pandemic preparedness. Within that broad consensus, CEPI will work to transform the world's ability to respond to new threats by investing in ground-breaking R&D, linking its investments with commitments to equitable access, and catalysing cooperation across a coalition of public and private sector partners.

CEPI has demonstrated its effectiveness through its response to COVID-19: in the space of five months CEPI created the world's largest portfolio of COVID-19 vaccines. The global R&D system, however, remains fragmented and the roles and responsibilities of key actors in this space must be clearly defined to maximise efficiency and ensure rapid response times. With CEPI acting as an organising force for global R&D collaboration and scientific innovation, the world is within reach of a future in which epidemic and pandemic diseases no longer pose an existential threat to humanity.

CEPI can help humanity substantially reduce, or even eliminate, the risk of epidemic diseases spiralling out of control like COVID-19. The dreadful human and economic cost of pandemics renders such a global insurance policy a bargain.



**True to its mission, when the COVID-19 crisis hit, CEPI stepped up to the mark. It established the world's largest portfolio of COVID-19 vaccines and co-created COVAX to enable equitable access to over 2 billion vaccine doses. The devastating impact of COVID-19 will continue to be felt for years to come, and while the global community rallies to end this pandemic, we must also act now to assemble the tools and infrastructure needed to ensure that we are prepared for the next 'Disease X'. CEPI's \$3.5 billion plan can not only achieve this goal, but it will also lay the groundwork for a future in which epidemics and pandemics no longer pose an existential threat to humanity.**

*Jane Halton, Chair of the Board, CEPI*





# CEPI's strategic priorities





# Prepare

## Prepare for known epidemic and pandemic threats

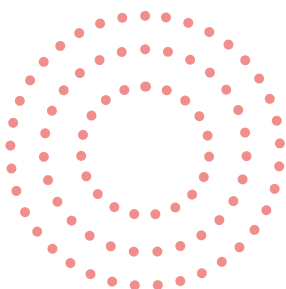
CEPI will prepare for known epidemics and pandemic threats by developing vaccines and promising biologics against the most prominent known threats, building on COVID-19 achievements and CEPI 1.0.



# Transform

## Transform the response to the next novel threat

CEPI will transform the response to the next novel threat by harnessing innovations in technology and systems to significantly reduce the global vulnerability to threats of novel pathogen outbreak.



# Connect

## Connect and enhance global collaboration

CEPI will enhance and expand global collaboration by connecting emerging infectious disease stakeholders to enable rapid countermeasure development, effective response and equitable access for those in need.

If the products developed with CEPI's funding are to realise their potential, they should flow through a system with pre-agreed governance, financing, allocation, and distribution mechanisms to govern their ultimate use. CEPI is already contributing to and helping shape a post-pandemic consensus, creating a well-prepared ecosystem able to react quickly without leaving anyone behind.



With  
\$3.5 billion  
CEPI will...



## Prepare

<b>COVID-19</b>	Fund late-stage clinical trials of promising vaccine candidates that can offer doses to COVAX, as well as investments in next generation approaches, including vaccines against emerging variants of concern
<b>Chikungunya</b> <b>Lassa Fever</b> <b>MERS</b> <b>Nipah</b> <b>Rift Valley Fever</b> <b>Ebola</b> <b>New priority pathogens</b>	Continue vaccine development of priority pathogens beyond what could be achieved in the first strategic cycle and expand support to late-stage (phase 2b/3) development towards licensure for priority pathogens with a clear unmet need where vaccines could have an impact.  Together with infectious disease experts, CEPI's Scientific Advisory Committee (SAC) and WHO, CEPI will continue to assess pathogens of concern and might consider adding up to two new priority pathogens to the portfolio, looking at the WHO Blueprint list of priority diseases and beyond
<b>Monoclonal antibodies</b>	Initiate the development of a monoclonal antibody programme for priority pathogens, focussing on certain parameters – ie, driving down costs and making these technologies accessible to all, with the aim of developing prophylactic monoclonal antibodies against priority pathogens that are ready for emergency use.
<b>Broadly protective Betacoronavirus vaccines</b>	Build on vaccine technologies validated in the COVID-19 response to develop clinical proof of concept for broadly protective SARS-COV-2 vaccines and broadly protective Beta-coronavirus vaccines

## Transform

<b>Disease X</b>	Further develop platforms and creating libraries of vaccine candidates, working with vaccine development partners to develop prototype vaccines for existing vaccine preventable diseases
<b>Enabling sciences programmes &amp; Manufacturing innovations</b>	Invest and scale critical enabling programmes to further accelerate vaccine development and deployment.  Development of manufacturing innovations that can accelerate epidemic and pandemic responses or enable the scaling of production of vaccines and other biological countermeasures, particularly in LMIC settings.

## Connect

<b>Manufacturing networks</b>	Strategic alliances with key manufacturers and coordinated investments in increasing global manufacturing capacity.
<b>Global research network</b>	Establish global networks for lab capacity, assays, and preclinical models that are critical for rapid vaccine development
<b>Alignment around a future target ecosystem</b>	CEPI aims to work with partners to agree upon key elements of the future preparedness and response ecosystem



The world  
needs CEPI  
more than ever

The world was caught off guard by the arrival of COVID-19 and it has struggled to come to grips with the unfolding pandemic. The scientific community rallied in response, displaying admirable solidarity as it united against this common threat. This community threw the full might of human ingenuity against one of the greatest public health threats to confront our species in more than a hundred years. But for all the ingenuity of the response, the pandemic also illuminated the inadequacy of the world's ability to detect emerging infectious threats and to effectively coordinate and mount rapid responses to slow the virus and prevent it from spreading globally.

These inadequacies in the global preparedness and response capabilities were known to the world long before the emergence of COVID-19. In the wake of the 2014-16 Ebola epidemic in Guinea, Liberia, and Sierra Leone, global health leaders recognised the urgent need to address these gaps.

The WHO created its R&D Blueprint for Action to Prevent Epidemics, the Global R&D Preparedness Monitoring Board (GPMB) was established as an independent body to monitor global preparedness for global health crises, and, in 2017, CEPI was formed to speed up the development and delivery of vaccines for potentially epidemic diseases.<sup>5,6</sup>

CEPI embarked on its mission with a handful of staff and initial pledges of \$460 million from Norway, Germany, Japan, Wellcome, and the Bill & Melinda Gates Foundation. By the end of 2020, over 30 countries along with multiple philanthropies and private organisations had pledged more than \$2.2 billion in funding for CEPI. To date, CEPI has made investments in 21 vaccine candidates against its priority pathogens, three rapid response platforms to develop vaccines against Disease X, 14 COVID-19 vaccine candidates for global use (11 of which have either received approval or remain in active development), and an array of cross-cutting, enabling science projects, all the while remaining lean in terms of staff numbers and overheads. Many of these diseases are principally regional threats (Lassa, MERS, Rift Valley Fever); several have expanded their range in recent years (Ebola, Nipah); and some have spread globally and are, or could be, regarded as pandemic (Chikungunya, COVID-19; appendix). While many of these pathogens have caused outbreaks of only limited size, the economic damage they cause can be enormous.

CEPI has also overseen a number of scientific "firsts", including the first phase 3 trial of a Chikungunya vaccine and the advancement of the first ever Nipah and Lassa virus vaccines into phase 1 trials (box 1). The advances that have been made in this short period simply would not have been possible without CEPI.

**BOX 1 :****CEPI supporting local partners to launch the largest ever epidemiological study of Lassa fever**

No licenced vaccine for Lassa fever exists, despite the fact that this haemorrhagic fever affects 300,000 people and kills an estimated 5000 people a year in West Africa.

CEPI identified significant gaps in epidemiological knowledge and understanding of disease transmission that would make evaluation of vaccine effectiveness challenging.

In response, in 2020, CEPI embarked on the largest ever epidemiological study of Lassa virus. It has partnered with seven local research institutions in Benin, Guinea, Liberia, Nigeria, and Sierra Leone where 23,000 participants will take part in a 2-year study to estimate the age-specific and sex-specific

incidence of both symptomatic and asymptomatic disease in these countries. To support the operation of this ground-breaking epidemiological study of the ground CEPI worked with the European and Developing Countries Clinical Trials Partnership (EDCTP) to invest in strengthening the clinical trial and laboratory capacity in partner countries. It also established an ambitious consortium of international partners—from academia and public sectors—such as MSF (France), The Robert Koch Institute (Germany), UK Public Health Rapid Support Team (UK), and many more, to establish the research infrastructure required to undertake the study including laboratory resources for sample analyses, field implementation, data management, and community engagement.

**The whole is greater than the sum of its parts**

As we emerge from the COVID-19 pandemic, we anticipate that many countries and groupings of countries will expand their investments in research on emerging infectious diseases and in establishing clinical trial networks, developing vaccine manufacturing capacity, and expanding regional collaborations. The UK, as part of its G7 presidency in 2021, will be working with global partners to implement a 5-point plan to prevent global health crises. This plan focusses on expanding research, surveillance, and manufacturing capacity, agreeing global protocols covering everything from information sharing to supplies of personal protective equipment for future health emergencies, and reducing trade barriers that have impeded the response. Meanwhile, Italy will lead the development of a global financing framework through the G20.<sup>7</sup>

But the global R&D environment remains fragmented and the path for products from the lab to the clinic is far from streamlined. The ongoing pandemic has shown the need to map out roles and responsibilities when it comes to preparedness and response. The response to the pandemic has



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COVAX

CEPI Gavi  
The Vaccine Alliance

unicef World Health Organization

ACTaccelerator  
ACCESS TO COVID-19 TOOLS

Delivery No: 187036220  
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Net Weight: 20.00  
Dimensions: 75.00 x 50.00 x 10.00  
Quantity: 1000 Vials  
Batch No: 4120257  
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Carton No: 0011  
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highlighted multiple challenges and gaps throughout the whole vaccine development process, including regulatory, clinical, and manufacturing hurdles; the constraints on enabling infrastructure (lab networks, preclinical model testing facilities); and challenges related to equitable access to and procurement of vaccines.

Few nations have the end-to-end capacity to translate basic research into products within their own borders. For example, some might have world-leading academic and research institutions but lack the manufacturing capacity to scale-up production of promising products for large-scale testing and distribution. Therefore, governments must look beyond their own borders, harness each other's strengths, and come together to establish a globally coordinated approach to epidemic and pandemic preparedness and response. The talent, technology, resources, and infrastructure required to achieve this vision exist in various places around the world, but political will is needed to enable harmonisation of these constituent parts of the global preparedness and response system.

### Harmonising the global R&D ecosystem

CEPI's global reach, organisational agility, and wide-ranging multisectoral connections proved to be critical in expediting COVID-19 vaccine R&D. As the world emerges from the COVID-19 pandemic, the development of a coordinated global approach to pandemic preparedness and response will be critical. An approach will be needed that pools financial firepower and weaves together the capabilities and expertise of public and private sectors in a way that amplifies the world's capacity to respond to future outbreaks. CEPI is now an established part of the global health and R&D ecosystems, has the prerequisite financial structures in place, and is well positioned to take on this role.

Over the first phase of operation, CEPI has forged partnerships with over 30 vaccine developers, manufacturers, and academic institutions. 30 countries, in addition to the European Commission, are now members of our coalition as well as the key philanthropic organisations the Bill & Melinda Gates Foundation and Wellcome Trust. It has also been supported by a number of private organisations. CEPI has established working relationships with major national regulators on all continents and has established strong operational relationships with key international health bodies such as the Africa Centre for Disease Control, Gavi, PAHO, UNICEF and WHO.

An independent review of CEPI's progress since it was established in 2017 highlighted that CEPI's ability to quickly pivot in the context of COVID-19 was a result of its flexible governance structure and a testament to the strong support for, and trust in, the organisation from investors and stakeholders.





CEPI is a key partner in helping to strengthen Africa's capacity to prevent, to detect, and to respond to emerging and reemerging disease threats. In short, we have an opportunity to address these gaps to help build resilience and capacity in low and middle income countries to deal with these threats. The time to invest is now. That is why the Africa Centres for Disease Control and Prevention welcomes and fully supports CEPI's mission to strengthen global epidemic and pandemic preparedness, including its commitment to support low and middle income countries in developing their R&D infrastructure and know-how needed to effectively tackle the threat of emerging and reemerging infectious diseases.

*John Nkengasong, Director of Africa CDC*



In particular, as CEPI embarks upon its next phase of operations, the report concluded that CEPI should further increase its role in ensuring that vaccines achieve licensure and are rolled-out in sufficient quantities, whether by directly investing or by playing a more catalytic role.

In the future envisioned by CEPI and its partners, an international system that enables the rapid development of vaccines will evolve: one that can simultaneously support R&D, promote manufacturing innovations and globally distributed manufacturing, and result in equitable distribution of vaccines and other countermeasures to all populations when pandemic threats emerge. The development of such a system, coupled with improved surveillance, detection, and rapid response, will substantially mitigate or even avert altogether the impact of future pandemics.

### **Strengthening health security**

#### **Addressing global R&D needs**

In its short history, CEPI has had an outsized influence in shaping the global R&D ecosystem, forging consortia where appropriate, developing new collaborations and injecting funding to jumpstart R&D when needed. It has also aligned programmes to complement the R&D efforts of its coalition partners.



The ability to rapidly develop vaccines for known and unknown diseases is critical if we're to prepare for and stop future epidemics. Supporting CEPI is the world's best chance to achieve this. Governments, industry and funders must all join in to ensure CEPI has funding it needs to protect the world.

There is no greater example of CEPI's ability to supercharge vaccine development, than the pivotal role it has played in developing a range of Covid-19 vaccines and ensuring these get to the whole world – not just the richest countries.

*Dr Jeremy Farrar, Director of Wellcome*



CEPI was initially conceived to address a number of critical gaps in the development of vaccines against emerging infectious diseases with epidemic potential but for which financial incentives to drive vaccine R&D were limited.

Even for vaccines for which there is global demand, the COVID-19 pandemic has shown that key market failures exist. Market forces do not always incentivise the development of products that meet the needs of all populations nor do they facilitate their equitable distribution when overall supplies are scarce. For example, the first COVID-19 vaccine approved following large-scale trials required an ultra-cold chain, which made it impractical for broad distribution in LMICs. Ensuring that vaccines and other biological countermeasures are developed that meet the needs of all segments of all populations in all geographies will be a core mission of CEPI going forward.

In response to the COVID-19 pandemic, CEPI played a pivotal role in the formation of COVAX and the Access to COVID-19 Tools (ACT) Accelerator. The ACT Accelerator brought together key public and private sector organisations to accelerate the development, procurement, and equitable distribution of vaccines, therapeutics, and diagnostics for the world. COVAX, the vaccines pillar of the ACT Accelerator, is co-led by WHO, Gavi, and CEPI, with UNICEF as lead delivery partner. COVAX aims to protect the most vulnerable populations, especially those living in LMICs who would normally be the last to benefit from innovative new vaccines.

It is clear that even in pandemic scenarios there is still an important role for public-sector financing. In a post-pandemic world, CEPI will leverage its unique position within the global health and R&D ecosystems to address these market failures, building on its proven track record of bringing together public-sector, private-sector, and academic partners across different geographies to pool resources, expertise, and capabilities to specifically accelerate the development of vaccines and vaccine-like technologies against pathogenic emerging disease threats.

In the near future, promising biological interventions such as monoclonal or gene-encoded antibodies could also be rapidly produced and given to patients to prevent or treat infection. Such interventions would provide protection even faster than vaccines, as the body does not need the time to generate an immune response. CEPI believes that such approaches could play an important role in speeding the response to emerging pathogens.

CEPI will therefore both support the development of vaccines against high-risk pathogens and make targeted investments in other biologics, initially with a focus on monoclonal antibodies. CEPI believes it can work to reduce the cost of these currently expensive medicines and advance manufacturing

innovations in this area to boost production, thereby enabling access for vulnerable populations.

By supporting CEPI, countries will be investing in strengthening and complementing the global R&D infrastructure needed to prepare and mount effective responses against epidemics and pandemics.

#### Protecting vulnerable populations

CEPI has committed up to \$705 million, including investments in support of enabling science, to develop more than 21 vaccine candidates against Ebola, Lassa, MERS, Nipah, Rift Valley Fever, and Chikungunya—diseases which disproportionately affect those living in LMICs (appendix).

CEPI will partner with LMICs at high risk from epidemic pathogens to address key gaps in clinical-trial capacity. We will strengthen clinical trial networks through engaging with national partners and product development partnerships on multiple continents, collaborating and leveraging synergies in networks that target epidemic infectious and neglected diseases. In doing so, CEPI will help to equip LMICs with the infrastructure and know-how to undertake epidemiological and clinical studies needed to advance vaccine development. At the same time, CEPI will work with organisations—like the Developing Countries Vaccine



**CEPI and its COVAX partners have begun to roll out the largest global vaccination campaign the world has ever seen. Ethiopia is a proud member of CEPI and fully supports its mission to speed up the development of vaccines against emerging epidemic threats.**

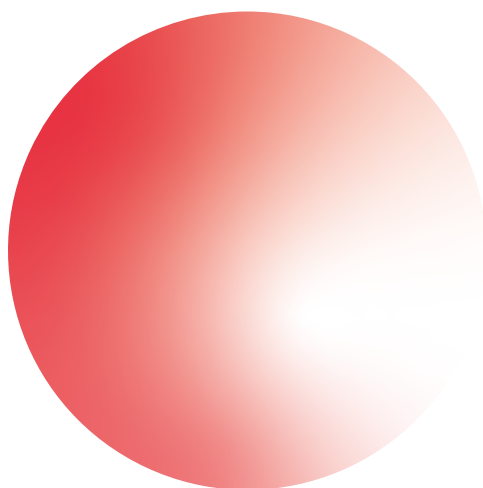
**We were the first African nation to partner and invest in CEPI and we hope over the next year many others will follow. We have seen the power of science to meet the challenge of this virus but that must go hand-in-hand with commitment to equitable access, because as we always say no one is safe until everyone is safe. Looking forward, Ethiopia will work with CEPI to strengthen Africa's capacity to prevent, detect, and respond to emerging infectious diseases.**

*H.E. Dr Lia Tadesse, Minister of Health of the Federal Democratic Republic of Ethiopia*



Manufacturers Network—to strengthen partnerships through which CEPI supports technology transfer and coordinates manufacturing capacity. Furthermore, CEPI will encourage partnerships between biotech companies and vaccine manufacturers to advocate for validated technologies and manufacturing innovations, which support the needs of LMICs, for example to enable lower cost-of-goods through innovation.

CEPI believes that by partnering with and supporting efforts of LMICs to strengthen their R&D capacity, we can contribute to improving their ability to prepare and rapidly respond to outbreaks, and consequently strengthen and speed up the world's ability to respond to emerging infectious disease threats.



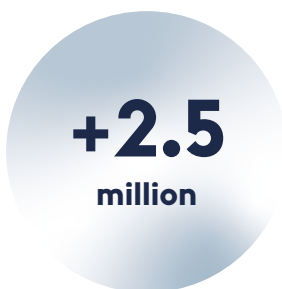


# Rising to the challenge of COVID-19

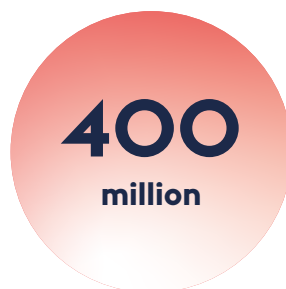
WHO declared COVID-19 a Public Health Emergency of International Concern on January 30, 2020 and a pandemic on March 11, 2020.<sup>8</sup> In the months that followed, COVID-19 spread worldwide. Within 3 weeks of the publication of the genome sequence CEPI had initiated vaccine development programmes with existing partners Curevac, Inovio and The University of Queensland and a new partnership with Moderna and the U.S. National Institute of Allergy and Infectious Diseases. In that same period, CEPI also established a ground-breaking new partnership with GSK to make their pandemic vaccine adjuvants, which can help boost vaccine-induced immune responses, available for use by CEPI's vaccine development partners.

Thanks to the support of CEPI's funders, the coalition has now committed over \$1.1 billion in support of COVID-19 vaccine development. As of November, 2021, CEPI has initiated 14 partnerships to develop COVID-19 vaccine candidates: 11 in clinical development, 2 reached emergency use listing and 2 terminated, with hundreds of million of doses made for COVAX procurement through CEPI's investment (table 1, box 2). All CEPI development partners have signed up to our equitable access principles, and we anticipate that multiple CEPI-supported vaccine candidates will be made accessible to the world through the COVAX Facility.

CEPI has built a deliberately diversified portfolio, composed of many different types of vaccine candidates. This approach ensures that the vaccine candidates do not share the same risks of failure. It is impossible to predict which vaccine candidates or technologies might fail at each stage. By investing in a wide range of vaccine technologies CEPI hedged its bets so as to increase its overall chances of success. CEPI's priorities in developing a vaccine portfolio have been speed, scale and access, and it has expert teams actively managing the portfolio, continuously assessing opportunities to expand or amend the portfolio to give CEPI the best possible chance of success.



Number of people killed due to COVID-19



Number of jobs lost as a direct result of the COVID-19 pandemic



Estimated reduction in global output by 2025 due to COVID-19

**TABLE I:**  
**CEPI's COVID-19 portfolio**

	<b>Phase of development  </b>	<b>Committed investment amount (USD\$)†</b>
<b>Biological E Limited (Protein antigen)</b>	Phase II/III	<b>Up to \$5 million</b>
<b>Clover Biopharmaceuticals (protein antigen)</b>	Phase II/III	<b>Up to \$397.4 million</b>
<b>CureVac (mRNA)</b>	Phase II/III*	<b>Up to \$15.3 million</b>
<b>Gritstone (Self-amplifying mRNA)</b>	Phase I	<b>Up to \$20.6 million</b>
<b>Inovio (DNA)</b>	Phase II/III	<b>Up to \$22 million</b>
<b>Institut Pasteur, Merck-Themis, University of Pittsburgh (Measles vector)*</b>	N/A	<b>Up to \$5 million</b>
<b>Novavax (Recombinant protein nanoparticle)</b>	Phase III	<b>Up to \$399 million</b>
<b>Moderna (mRNA)</b>	Phase III/WHO EUL granted	<b>Up to \$1 million</b>
<b>SK bioscience (Recombinant protein)</b>	Phase III	<b>Up to \$210 million</b>
<b>University of Hong Kong Live attenuated</b>	Phase I	<b>Up to \$5.4 million</b>
<b>University of Oxford/ AstraZeneca (Viral vector)</b>	Phase III/WHO EUL granted	<b>Up to \$383 million</b>
<b>University of Queensland / CSL* (Recombinant protein)</b>	N/A	<b>Up to 4.5 million</b>
<b>VBI Vaccines (Enveloped-virus like particle)</b>	Phase I	<b>Up to \$33 million</b>
<b>Zerun Bio (Chimeric protein vaccine)</b>	Phase I/II	<b>Up to \$13.1 million</b>

\*Funding discontinued.<sup>9,10</sup> †Funds committed at the time partnering agreements were established, unless otherwise stated. Actual investments are made in tranches, dependent on completion of pre-specified project milestones. ‡Total funds invested in the project. ||Data correct as of November, 2021.



## Scaling up and scaling out manufacturing

Early in the pandemic, CEPI urged global investment from developed and developing countries to increase manufacturing capacity before efficacy data were available, because this was the only way to enable the world to move quickly as soon as a vaccine was shown to be safe and effective. This involved substantial financial risk (because predicting exactly which vaccine will be successful from the outset is not possible) but it was a critical element in accelerating the pace of vaccine development.

To boost global manufacturing capacity early, CEPI stepped up and made a number of investments including agreements with Novavax, The University of Oxford and AstraZeneca, Clover Biopharmaceuticals, and University of Queensland and CSL to begin manufacturing millions of doses of their COVID-19 vaccine candidates, which—if proven safe and effective—were to be made available for globally fair allocation.

### BOX 2 :

#### How CEPI collaborates with vaccine developers: a COVID-19 case study

Prior to the COVID-19 pandemic—and in recognition of the threat posed by Disease X and coronaviruses in particular—CEPI had allocated over \$50 million to develop vaccine platform technologies that could enable the development of rapid-response vaccines against newly emerging pathogens and over \$140 million to develop vaccines against MERS, a virus related to SARS-Cov-2. CEPI redeployed most of its MERS and platform technology partners to work on COVID-19. Notably, CEPI established a collaboration with the University of Oxford in 2018 to develop a vaccine against MERS using their ChadOx vaccine platform.

In response to COVID-19, CEPI quickly provided additional funding to enable the University of

Oxford to adapt this platform technology to develop a vaccine candidate against COVID-19. To scale manufacture of their COVID-19 vaccine candidate, the University of Oxford subsequently partnered with AstraZeneca, who committed to producing the vaccine on a not-for-profit basis during the pandemic period.

To enable global access to this vaccine candidate, CEPI then invested a total of up to \$383m to support the technical transfer of vaccine production technology to manufacturing sites predominantly in Europe, thereby creating additional manufacturing capacity for this vaccine and secured a total 300 million doses of vaccine for globally fair allocation.

CEPI also undertook a global assessment of vaccine manufacturers—in collaboration with the Bill & Melinda Gates Foundation, The Clinton Health Access Initiative, and PATH—to determine where manufacturing capacity was available in the world and how CEPI could facilitate manufacturing in multiple geographical locations.<sup>11</sup>

As a hedge against the unpredictable risk of vaccine nationalism, CEPI ensured that the manufacturing partnerships it established were in different regions. To further mitigate against the risk of one country monopolising supply, CEPI also added provisions into its vaccine development contracts, with a manufacturing component, that required its partners to direct all CEPI-funded doses to “a global procurement and allocation entity”. That entity would later become established as COVAX.

### **Adapting to SARS-CoV-2 variants**

To minimise variation in assessment and allow for head-to-head comparisons between promising COVID-19 vaccine candidates, CEPI launched a centralised lab network, open to all COVID-19 vaccine developers, to standardise the evaluation of COVID-19 vaccine candidates and allow for researchers to identify the most successful potential vaccines.

The work of CEPI’s centralised labs will become increasingly essential as vaccines become more widely available, because the way that clinical trials of COVID-19 vaccines are conducted will change. One of the aims of the centralised lab network is to establish reliable markers of immunity, which are critical if researchers are to assess the efficacy of COVID-19 vaccines. Our network of labs will help to harmonise evaluation of the immune responses generated by multiple COVID-19 vaccine candidates. This will allow researchers to establish reliable markers of immunity—like how high antibody levels need to be to neutralise COVID-19—which will help regulators assess the efficacy of various vaccine candidates in the absence of data from placebo-controlled trials.

In parallel, CEPI also launched its Agility programme to assess the impact of emerging viral strains of COVID-19 on the effectiveness of COVID-19 vaccines.<sup>12</sup> This programme is centred on a taskforce that includes the GISAID Initiative, Public Health England, and the National Institute for Biological Standards and Control. A first-of-its-kind collaboration, these organisations are working together to strengthen real-time global tracking and testing of COVID-19 virus sequences, to assess the impact of new viral strains on the immune response generated by various vaccine candidates.<sup>13</sup>

## Creating COVAX to tackle the COVID-19 pandemic

On May 4, 2020, CEPI, alongside Gavi and the WHO, launched COVAX—the vaccines pillar of the ACT Accelerator—with the aim of ending the acute phase of the pandemic by the end of 2021.<sup>14</sup> It represented the only global plan to deliver fair, equitable and necessary access to vaccines for every country that participates. This initiative was specifically designed to share the risks and benefits across all of the participating economies, pooling financial resources to purchase vaccines at scale, sharing the risks associated with developing vaccines, and investing up-front in manufacturing so that vaccines are ready to be equitably distributed as soon as they are licensed. The establishment of COVAX represents the largest multilateral undertaking since the Paris Climate Agreement.<sup>15</sup>

The ultimate goal of COVAX was to minimise suffering and death, keep borders open and promote the restoration of normal economic activity around the world by making 2 billion doses of vaccine available by the end of 2021. This would be sufficient to immunise healthcare workers and the most vulnerable segments of the population of each participating country and hasten the end of the acute phase of the pandemic.

By December 2020, COVAX had put agreements in place to enable access to nearly 2 billion doses of several promising vaccine candidates. COVAX began delivering vaccines to participating countries in February, 2021, and anticipates providing 2 billion doses in the first quarter of 2022. Both the ACT Accelerator and COVAX are promising initiatives and, while there is room for improvement, will likely serve as models for how to address future development and distribution challenges in the future.





No time  
to lose

Despite the ongoing traumas of COVID-19, we need to begin preparing now for the next pandemic. We need to learn from successes but also our failures, identifying the gaps in our global R&D system and fixing them, coming up with new ways to ensure that financing is available for rapid pandemic responses, and leveraging the strong public interest and political will in the wake of COVID-19 to make all of this happen.

Our globally connected world has made us vulnerable to the rapid spread of new zoonoses and the emergence of another pandemic disease is just a matter of time. Rapid urbanisation, deforestation, intensive agriculture, livestock rearing practices, and globalisation are increasing opportunities for animal-to-human contacts and for human-to-human transmission of disease on a global scale.<sup>16</sup> Urbanisation in particular is creating greater potential for epidemics and even pandemics.<sup>17</sup> More than half of the world's population now lives in cities, and just about every country on the planet is becoming more urbanised.<sup>18,19</sup>

While it is impossible to prepare a vaccine for every virus ahead of time, we can prepare a global infrastructure that is ready to respond rapidly and ensures vaccines, and other biological countermeasures, are distributed fairly to all populations in need.

Investment in CEPI will improve the world's ability to mitigate and potentially avert any future pandemic and is thus an insurance policy with enormous benefits, not least potentially saving millions of lives and preventing or significantly reducing the economic, social, and political fall-out of such a calamity.

CEPI has become an irreplaceable part of the global R&D ecosystem, filling a unique niche in accelerating vaccine development against emerging infectious diseases. In collaboration with its partners, CEPI will build on the advances it has made in this period to transform the world's ability to prepare and respond to epidemic and pandemic diseases, while strengthening the R&D and response capacities of countries disproportionately affected by these threats.

CEPI has a grand vision for the world: a world in which epidemics and pandemics are no longer a threat to humanity. CEPI has already made great strides towards this ambitious goal.

The vaccine R&D and manufacturing developments that CEPI has helped to advance during the COVID-19 pandemic will revolutionise vaccinology. CEPI is committed to realising the benefits of this progress to strengthen our preparedness against known and future threats.



With these new tools in hand, we can envision a world in which vaccines and other countermeasures can be developed in just 100 days. CEPI's expertise will also be critical in advancing other promising biological countermeasures, like monoclonal antibodies, which will serve as important adjuncts to the world's preparedness and response capabilities.

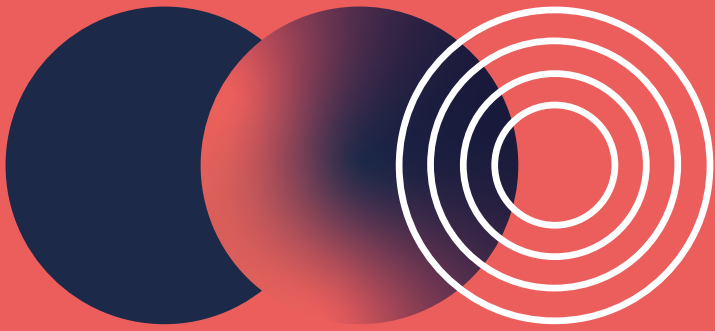
CEPI's unique contribution to global preparedness is its demonstrated ability to accelerate vaccine R&D while linking its investments in innovation with commitments to equitable access.

**The world now stands at a crossroads. Do we continue to walk the path of panic and neglect that has characterised the response to and aftermath of previous epidemics and pandemics—or do we come together to break that cycle for the benefit of all of humanity?**

CEPI's goal is to work with and through partners to systematically reduce the threat posed by future epidemics and pandemics and ensure that these benefits are shared by all. To accomplish this goal, we are seeking to raise \$3.5 billion to support planned activities over the next 5 years. Applying these resources to our ambitious but focussed R&D agenda will have transformative effects and could help prevent millions of deaths and tens of trillions of dollars in future costs to the global economy.

The course of human civilisation has been shaped by opportunistic pathogens. Now, for the first time in human history, we are within reach of capabilities that could neutralise the threat such pathogens present. CEPI and its partners, working through global networks and in solidarity with scientists around the world, will steer us towards a future in which epidemic and pandemic diseases no longer present an existential risk to humanity.

We must act now. There is no time to lose.



# Appendix



## CEPI's priority-pathogen vaccine portfolio excluding COVID-19 investments

The global need for CEPI was recognised after the devastating Ebola epidemic of 2014-16 in Guinea, Liberia, and Sierra Leone, which killed more than 11,000 people and had an economic and social burden of over \$53 billion.<sup>20</sup> The world's response to this crisis fell tragically short. A vaccine that had been under development for more than a decade was not deployed until over a year into the epidemic. That vaccine was shown to be 100% effective, suggesting that much of the epidemic could have been prevented. It was evident that the world needed a better system to speed the development of vaccines against known epidemic threats.

CEPI was launched at Davos in 2017, by the governments of Norway and India, the Bill & Melinda Gates Foundation, the Wellcome Trust, and the World Economic Forum, as the result of a consensus that a coordinated, international, and intergovernmental plan was needed to develop and deploy new vaccines to protect against epidemics caused by emerging infectious diseases.

CEPI has prioritised a number of pathogens in view of the market failures to accelerate vaccine development against these threats and because of the potential health, social, and economic damage they might inflict on vulnerable populations, especially those living in LMICs. In addition to CEPI's ongoing response to COVID-19, these priority pathogens include Ebola, MERS, Nipah, Chikungunya, Lassa Fever, and Rift Valley Fever.

## Ebola

In addition to the substantial direct health and economic impacts of the 2014-16 Ebola epidemic in Guinea, Liberia, and Sierra Leone, local resources were also diverted from basic health care and government services to the outbreak, resulting in serious under-provision of health and social care. An estimated 3.5 million untreated cases of malaria and nearly 11,000 additional deaths from HIV/AIDS, tuberculosis, and malaria were an indirect result of the diversion of health resources.<sup>21</sup> Economic growth also slowed significantly, largely due to reduced financial investments and productivity levels during and after the outbreak.

In 2018-19, the DRC faced the second worst Ebola outbreak in history. In response to the outbreak, CEPI established an international consortium of global health partners to launch a trial of an Ebola vaccine (Ad26.ZEBOV/MVA-BN-Filo; Johnson and Johnson) in the DRC in October, 2019. The distribution of this vaccine candidate, in a clinical-trial setting, allowed the collection of important data in a real-world setting on the administration of a vaccine that could be used to protect multiple vulnerable populations.

As part of the consortium, Janssen Vaccines (a Johnson and Johnson company) agreed to deliver up to 500,000 doses of the vaccine regimen for those in communities near the outbreak who were considered at risk, as determined by the DRC authorities and consortium partners, at a time when it was unclear whether the primary ring vaccination strategy would be able to bring the outbreak under control. Fortunately, in late June, 2020, after an outbreak lasting some 23 months, the epidemic was brought under control and declared over.

CEPI brought together an international group of funders for this outbreak response, and secured funding from the European Union, the UK Government, Wellcome and the Paul G. Allen Family Foundation.<sup>22</sup> As of January, 2020, over 20,000 people have been vaccinated.

	Target pathogen (phase of development)	Committed investment amount‡
<b>2017 to 2020</b>		
<b>Auro Vaccines (USA) and PATH (USA)</b>	Nipah virus (phase I)	<b>Up to \$25.0 million</b>
<b>Colorado State University (USA)</b>	Rift Valley Fever (preclinical)	<b>Up to \$9.5 million</b>
<b>Curevac (Germany)*</b>	Lassa virus (preclinical) Rabies virus (preclinical)† Yellow Fever (preclinical)†	<b>Up to \$34.0 million</b>
<b>Emergent Biosolutions (USA)</b>	Lassa virus (preclinical)	<b>Up to \$36.0 million</b>
<b>IAVI (USA)</b>	Lassa virus (phase I)	<b>Up to \$64.4 million</b>
<b>Imperial College London (UK)*</b>	H1N1 influenza (preclinical)† Rabies virus (preclinical)† Marburg virus (preclinical)	<b>Up to \$8.4 million</b>
<b>IDT Biologika (Germany)</b>	MERS (preclinical)	<b>Up to \$36.0 million</b>
<b>Inovio Pharmaceuticals (USA)</b>	Lassa virus (phase Ib) MERS (phase 2)	<b>Up to \$56.0 million</b>
<b>IVI (South Korea) and Bharat Biotech (India)</b>	Chikungunya virus (phase I)	<b>Up to \$14.1 million</b>
<b>Janssen Vaccines (Netherlands)</b>	Ebola virus (licensed)	<b>\$25.7 million</b>
<b>Merck Vaccines (USA)</b>	Ebola virus (licensed)	<b>\$1.5 million</b>
<b>Public Health Vaccines (USA)</b>	Nipah virus (preclinical)	<b>Up to \$43.6 million</b>
<b>Themis Bioscience (Austria)</b>	Lassa virus (phase I) MERS (preclinical) Chikungunya (phase 3)	<b>Up to \$58.5 million</b>
<b>University of Oxford (UK) and Janssen Vaccines (Netherlands)</b>	Lassa virus (preclinical) MERS (Phase I) Nipah virus (preclinical)	<b>Up to \$19.0 million</b>
<b>University of Queensland (Australia)*</b>	Influenza (preclinical)†, MERS (preclinical), Respiratory syncytial virus (RSV; preclinical)†	<b>Up to \$10.6 million</b>
<b>University of Tokyo (Japan)</b>	Nipah virus (preclinical)	<b>Up to \$31.0 million</b>
<b>Valneva SE (France)</b>	Chikungunya virus (phase 3)	<b>Up to \$23.4 million</b>
<b>Wageningen Bioveterinary Research (Netherlands)</b>	Rift Valley Fever virus(preclinical)	<b>Up to \$12.5 million</b>

Data in this table are correct as of November, 2021 \*Investment part of “Disease X” platform technology development. †Non-priority pathogens selected to assess platform technology. ‡Funds committed at the time partnering agreements were established, unless otherwise stated. Actual investments are made in tranches, dependent on completion of pre-specified project milestones.

## MERS

While the 2014–16 Ebola epidemic, which caused more than 28,000 infections and 11,000 deaths, resulted in a substantial overall social and economic burden (of around \$1.8 million per case), the impact of a limited outbreak of MERS in South Korea in 2015 was staggering, exceeding \$50 million per case.<sup>23</sup>

In May 2015, a South Korean man returning from the Middle East was treated in several healthcare facilities, infecting at least 26 people, before he was diagnosed with MERS. The epidemic that ensued accumulated 186 cases overall, led to 38 deaths, prompted the closure of more than 2,700 schools, and resulted in the quarantine of nearly 17,000 people before it was brought under control some 2 months later. Health researchers estimated that the total cost, including losses in retail sales and tourism, approached \$10 billion.<sup>24</sup>

Prior to the COVID-19 pandemic, CEPI had developed a robust portfolio of MERS vaccine candidates and related enabling science projects and committed more than \$140 million to MERS vaccine development. These investments laid the groundwork for our rapid response to COVID-19 and enabled us to pivot four of the projects, including the Oxford vaccine, to rapid COVID-19 vaccine development.

## Nipah

Nipah virus and the closely related Hendra virus have caused only a handful of outbreaks in Asia and Oceania, but the potential for much larger exposure is considerable, since more than 2 billion people live in parts of the world where *Pteropus* bats—the natural hosts of these viruses—are found.<sup>25</sup>

The first and largest known outbreak of Nipah virus began in September 1998 when swine fell ill in the village of Ipoh in Perak, Malaysia. Soon the farmers themselves were falling ill, falling victim to a frightening combination of brain inflammation and pneumonia. The outbreak was initially attributed to Japanese encephalitis and early control measures focussed on anti-mosquito fogging and vaccination of pigs against Japanese encephalitis. By February, the outbreak had spread south to Sikimat, Sungai Nipah village, whence the virus took its name; and by mid-1999, some 265 cases and 105 deaths had occurred in Malaysia and the disease had spilled across the border into Singapore, where 11 abattoir workers fell ill (leading to one additional death). In the effort to contain the outbreak, the Malaysian army was deployed to cull over a million pigs, reducing the national herd by perhaps as much as one half and leading to the collapse of the pig farming industry in the most affected areas. The epidemic was estimated to have had a wider economic impact of nearly \$600 million.<sup>26</sup>

Since this first outbreak, in a pattern similar to that observed with Ebola, Nipah has gradually expanded its range. The virus next emerged in Bangladesh and West Bengal in 2001, and over the past two decades has infected more than 300 people in these regions. In 2018, Nipah emerged on India's southwest coast, causing a small epidemic in the state of Kerala, more than 3,000km from Malaysia, where the first outbreak was reported 20 years previously. In 2011, Nipah gained notoriety as the prototype for the fictional MEV-1 virus in the film *Contagion*.

CEPI has committed over \$100 million to Nipah research and currently supports four early-stage vaccine candidates. One vaccine candidate, based on the licensed equine Hendra vaccine Equivac HeV, is now being tested in a Phase 1 clinical trial and the other three are completing preclinical studies.



## Chikungunya

A virus with an even wider geographical range is Chikungunya. Today, well over a billion people live in areas where Chikungunya outbreaks occur.

Despite the large outbreaks and significant consequences of this disease, there is currently no specific antiviral drug treatment nor are any vaccines licenced for human use against this virus. Chikungunya virus was first identified in Tanzania in 1952, with sporadic outbreaks of the disease reported subsequently across Africa and Asia.<sup>27</sup> In 2004, the disease began to spread quickly, causing large-scale outbreaks around the world. Since the re-emergence of the virus, the total number of cases has been estimated at over 3.4 million in 43 countries.<sup>28</sup>

Climate change could further amplify the threat posed by Chikungunya. As the climate warms, more areas across the world will become habitable for the mosquito vectors that transmit the virus, thereby increasing the size of the human population at risk of infection. For example, in 2007, an outbreak of Chikungunya virus infections was declared for the first time in Europe with more than 200 human cases reported in Italy.<sup>29</sup> Since 2014, in the USA, local-transmission of the virus has been reported in Florida, Puerto Rico, Texas and the U.S. Virgin Islands.<sup>30</sup>

In 2019, and in partnership with the European Union Horizon 2020 fund, CEPI partnered with Valneva (France), Bharat Biotech (India) and International Vaccine Institute (South Korea), and Themis Bioscience (Austria) in three separate Chikungunya vaccine programmes. Valneva initiated Phase 3 clinical trials of their vaccine—the last stage of testing before licensure—in September 2020.

## Lassa Fever

Before the emergence of COVID-19, Lassa Fever was the priority pathogen with the greatest annual incidence. An estimated 100,000–300,000 cases of Lassa Fever, with approximately 5,000 related deaths, are thought to occur every year in West Africa, although most are undiagnosed. In 2018, the Nigeria Centre for Disease Control reported the largest ever number of cases in Nigeria, with over 600 confirmed cases and over 170 deaths.

There are high death rates among those requiring hospital admission, with frequent nosocomial transmission to staff and concomitant disruption of health services. The socioeconomic impact of Lassa Fever extends beyond the acute infection, with many recovering patients unable to care for themselves and their dependants. Hearing loss is frequently observed as a sequela of clinical or subclinical infection and produces lifelong disability.<sup>31</sup>

CEPI has invested in the development of six Lassa vaccine candidates. In May, 2019, Inovio Pharmaceuticals advanced the first ever Lassa vaccine into phase 1 trials, with support from CEPI.<sup>32</sup> CEPI now has two candidates in phase 1 trials with its developers Inovio and Themis Bioscience. Inovio's vaccine candidate has also entered phase 1 testing in West Africa—these are the first Lassa vaccine trials on the continent.<sup>33</sup> To accelerate Lassa vaccine development, CEPI has launched the largest epidemiological studies of the virus ever undertaken – the ENABLE Lassa research programme.

CEPI has committed a total of \$263 million to its Lassa programmes, almost \$30 million of which is allocated to enabling science work, including the epidemiological studies.

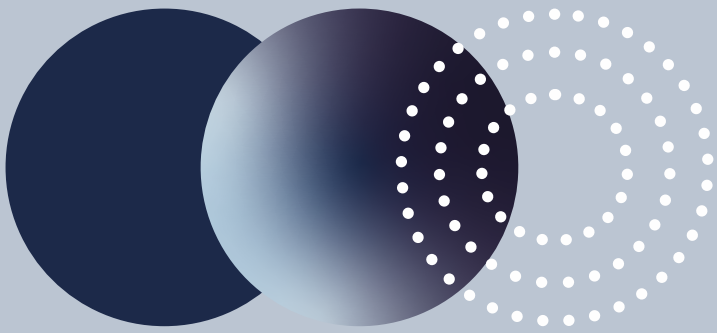
### **Rift Valley Fever**

Rift Valley Fever was first identified in 1931 during an investigation into an epidemic among sheep on a farm in the Rift Valley of Kenya. Multiple outbreaks have since been reported across the African continent and in Saudi Arabia and Yemen. Rift Valley Fever mainly affects people living in pastoral communities in low-income and middle-income countries.

The US CDC has classed Rift Valley Fever as a category A bioterrorism agent, given its potential to devastate large-scale agricultural economies and cause substantial social disruption.<sup>34</sup>

The United States, the Netherlands, the United Kingdom, and many locations in the European Union have been identified as potential points for emergence of Rift Valley Fever due to presence of mosquito species capable of transmitting the virus and extensive livestock economies and trade. Changes in climate and seasonal extremes might also increase the risk Rift Valley Fever might be introduced to these areas.<sup>35</sup>

CEPI has two Rift Valley Fever vaccine candidates in its portfolio. Both are undergoing preclinical studies.



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